

BRIEF COMMUNICATION

Risk of Transfusion-Associated Transmission of Human Herpesvirus 8

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Human herpesvirus 8 (HHV8), also known as Kaposi's sarcoma herpesvirus, causes Kaposi's sarcoma (1) and is associated with body cavity-based lymphomas and multicentric Castleman's disease (2,3). HHV8 is spread sexually (4,5), but other routes of transmission probably exist because, in some cases, infection has been shown to be acquired in childhood in HHV8-endemic areas, such as Mediterranean Europe and sub-Saharan Africa (6–8).

An unresolved question with public health implications is whether blood transfusions can transmit HHV8. HHV8 can be identified in circulating lymphocytes from healthy blood donors (9,10), although the proportion of infected donors with viremia is unknown. Cytomegalovirus, another cell-associated herpesvirus, is readily transmitted via blood transfusion (11), and both HHV8 and cytomegalovirus are transmitted through solid organ transplantation (12,13). However, no study to date has documented HHV8 transmission through transfusion; the only study to examine this question directly found no transmission of HHV8 from 14 HHV8-seropositive donors (14). Furthermore, HHV8 infection is relatively rare in frequently transfused groups, such as hemophiliacs (14) and thalassemia or sickle cell anemia patients (15). Determining whether transfusions may transmit HHV8 has been difficult because HHV8 infection is fairly uncommon among many donor populations [e.g., 0%–5% seroprevalence in the United States (16–18), in the U.K. (17), and in the Caribbean (19)].

To determine whether blood transfusions can transmit HHV8, we evaluated

individuals in the Jamaica Transfusion Study (20). Between May 1987 and September 1988, blood donors and recipients of units from these donors were enrolled in a study of human T-cell lymphotropic virus-I (HTLV-I) transfusion-associated transmission in Kingston, Jamaica (20). Donors were screened for HTLV-I antibodies by use of several investigational assays, but some units from HTLV-I-seropositive donors were transfused before infection was identified. Through standard blood bank screening, all donors had tested negative for infection with human immunodeficiency virus-1 (HIV), hepatitis B, and syphilis. In addition, donors denied previously using intravenous drug use or engaging in high-risk sexual behavior. This study was approved by institutional review committees at the National Cancer Institute and the University of the West Indies, and participating individuals provided their written informed consent.

For the present examination of HHV8 transmission risk, we tested plasma or serum samples (stored at –70 °C) from this prior study. We measured HHV8 serostatus with an enzyme immunoassay (EIA) that uses a lysate of sucrose-purified whole virus obtained from HHV8-infected KS-1 cells (Advanced Biotechnologies, Inc., Columbia, MD) (21). This assay detects antibodies to most structural and non-structural antigens present in HHV8 virions and has 75%–100% sensitivity (for detecting seroreactivity in persons with Kaposi's sarcoma) and 90%–100% specificity (21,22).

Twenty-seven (2.7%) of 1010 donors were HHV8 seropositive. Seroprevalence was similar for men and for women and increased with age (Table 1). HHV8 seroprevalence did not differ between HTLV-I-seropositive and HTLV-I-seronegative donors (Table 1).

Nineteen recipients of units from these HHV8-seropositive donors had stored post-transfusion samples available and could thus be evaluated (Table 2). Fourteen recipients received one seropositive unit, four received two, and one received four. Transfused units included seven packed red blood cell units, four platelet units, five whole-blood units, seven fresh-frozen plasma units, and three cryoprecipitate units.

For each evaluable recipient, we tested two post-transfusion specimens, obtained a median of 355 days after the

last HHV8-seropositive transfusion (range, 29–1367 days), for HHV8 antibody. Only one recipient had antibodies to HHV8. However, before transfusion, this subject (No. 3013) was already HHV8 seropositive and had HHV8 DNA detected in peripheral blood by polymerase chain reaction, indicating that infection antedated transfusion (data not shown). None of the other 18 recipients were seropositive following transfusion (0%; exact 95% confidence interval [CI] = 0%–15%). The transmission risk per HHV8-seropositive unit was 0% (exact 95% CI = 0%–11%).

One donor whose serology indicated co-infection with HHV8 and HTLV-I provided packed red blood cells to a recipient who was seronegative to both viruses before transfusion (subject No. 800). The recipient acquired HTLV-I from this transfusion (20) but remained HHV8 seronegative.

Our findings of a lack of transmission of HHV8 through transfusion confirm observations from the Transfusion Safety Study, in which none of 14 recipients of HHV8-seropositive blood transfusions developed infection (14). These two studies, which together comprised 32 seronegative transfusion recipients, suggest that transfusion-associated transmission occurs infrequently (exact 95% CI for transmission risk = 0%–9% per individual transfused). Single transfusions that transmitted HTLV-I (present study) or HIV [Transfusion Safety Study (14)] but not HHV8 provide further evidence that HHV8 is not efficiently spread via transfusion.

One reason for the lack of transfusion-associated transmission may be that, in healthy blood donors, cell-mediated immune responses reduce circulating virus levels. Among healthy blood donors and HIV-infected per-

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Table 1. Characteristics of seropositive blood donors*

Characteristic	No. of HHV8-seropositive donors/total No. (%)†	P‡
Sex		.27
Men	20/854 (2.3)	
Women	6/137 (4.4)	
Age quintile, y		.001
18–21	2/151 (1.3)	
22–25	2/235 (0.9)	
26–29	3/187 (1.6)	
30–35	8/207 (3.9)	
36–63	11/211 (5.2)	
HTLV-I status		.58
Seropositive	3/69 (4.3)	
Seronegative	23/932 (2.5)	

*HHV8 = human herpesvirus 8; HTLV-I = human T-cell lymphotropic virus-I.

†Sex, age, and HTLV-I status were not available for some subjects; therefore, categories do not add to 1010, the total number of donors evaluated.

‡Two-sided *P* values were calculated on the basis of chi-squared tests (for sex and HTLV-I status) or coefficients from logistic regression (for trend across age quintiles).

sons, the probability of detecting circulating HHV8 is inversely related to CD4 count (23). Blackburn et al. (10), who found HHV8 in circulating B lymphocytes in multiple samples from one blood donor, noted that this donor had a persistently low CD4:CD8 ratio.

The paucity of B lymphocytes accompanying most types of transfusion may also contribute to low transmission risk. HHV8 may circulate in blood

largely within mononuclear cells (23,24) and predominantly within B lymphocytes (10). For red blood cell transfusions, transmission risk may be reduced through routine procedures that remove most circulating B lymphocytes (25). Similarly, acellular blood products have few lymphocytes and might convey little risk. For HTLV-I, transmission risk declines markedly when blood components are stored for more than 1 week (20), but storage time cannot explain the lack of HHV8 transmission because many units were transfused after being stored for only a few days (Table 2).

In this study, we may have been limited by the performance of currently available serologic assays for HHV8. We might have missed instances of HHV8 transmission because some HHV8-infected donors or recipients may not have been detected by the EIA. Also, given the few HHV8-seropositive donors, we pooled together all types of blood components in examining transfusion risk. Cellular blood components, especially whole blood, may carry a higher transmission risk, but we had insufficient power to examine this hypothesis.

Available evidence suggests that blood bank screening for HHV8 infection is not currently indicated. First, donor infection is relatively uncommon outside HHV8-endemic areas (16–18). Second, as we document, blood components from HHV8-infected donors ap-

parently carry low transmission risk. Third, existing HHV8 serologic assays may not perform well enough for screening because available tests might miss many HHV8-infected units or incorrectly label HHV8-uninfected units as infected. Nonetheless, the issue of transfusion-associated transmission of HHV8 should be examined further in studies of additional populations, particularly when improved methods for detecting HHV8 infection become available.

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Table 2. Characteristics of recipients of transfusions from human herpesvirus 8 (HHV8)-seropositive donors*

Subject identification No.	Diagnosis	Sex	Age, y	Type(s) of HHV8-seropositive units received	Storage time of transfused units, d
145	Bladder cancer	Male	75	PRBC	1
193	Aplastic anemia	Male	36	PLT, PLT, PLT, PLT	0, 1, 1, 5
387	Trauma	Male	26	WB	2
508	Burns	Male	18	PRBC	NA
800	Preeclampsia	Female	29	PRBC	3
844	Foot abscess	Female	58	WB	12
992	Trauma	Male	20	FFP	33
1477	Peritonitis	Male	25	FFP	22
2266	Menorrhagia	Female	28	PRBC	2
3013	Myelofibrosis	Female	66	PRBC	9
3217	Colon cancer	Female	85	WB	46
3413	Hemophilia	Male	25	CRYO	56
3459	Hypogammaglobulinemia	Male	19	FFP, FFP	3, 45
3578	Perforated appendix	Male	36	FFP, FFP	17, 30
3687	Esophageal varices	Male	79	WB	20
4125	Upper gastrointestinal bleed	Male	43	FFP, PRBC	3, 26
4334	Peptic ulcer	Male	36	PRBC	19
5384	Premature labor	Female	15	WB	8
6923	Hemophilia	Male	23	CRYO, CRYO	3, 4

*HHV8 = human herpesvirus 8; PRBC = packed red blood cells; PLT = platelets; WB = whole blood; FFP = fresh-frozen plasma; CRYO = cryoprecipitate; and NA = not available.

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NOTES

Editor's note: D. V. Ablashi is an employee of and owns stock in Advanced Biotechnologies, Inc.; H. Eastman is an employee of the company but does not own stock. Advanced Biotechnologies, Inc., manufactures an enzyme immunoassay kit used in the study.

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